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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/812,393	03/05/1997	LINDA A. SHERMAN	313332000100	2284

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EXAMINER	
WILSON, MICHAEL C	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/812,393	SHERMAN ET AL.	
	Examiner	Art Unit	
	Michael C. Wilson	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11-24-04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim 22 has been added. Claims 1-5 and 22 are pending and are under consideration in the instant office action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Objections

In claim 1, step a), the immunization should result in the production of human HLA restricted CTL to more accurately reflect the nature of the invention.

Claim Rejections - 35 USC ' 112

Claims 1-5 and 22 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The limitation of "a non-human TCR specific for a tumor-associated antigen (TAA) and restricted by HLA" as newly amended in the preamble of claim 1 does not have support on pg 3, lines 8-18. The specification states

> "...the invention relates a method to prepare an isolated nucleic acid molecule comprising a nucleotide sequence encoding at least one of the variable regions of the α and β chains of a non-human TCR which TCR is human HLA-restricted and specific for a tumor-associated antigen, which method comprises cloning or amplifying a nucleic acid molecule containing said encoding nucleotide sequence from the CTL prepared by a method which comprises immunizing a transgenic non-human vertebrate which is modified so as to express at least one human HLA antigen with said tumor associated antigen (TAA) so as to effect the

production in said mouse of cytotoxic T lymphocytes which display human HLA-restricted TCR specific for said TAA."

While the specification contemplates obtaining TCRs from any non-human vertebrate restricted by human HLA, the specification does not contemplate obtaining non-human TCR restricted by any HLA as broadly claimed. Support for the breadth of TCR cannot be found on pg 5, lines 4-5 and 23-25; pg 6, lines 16-22; pg 6, line 28, to pg 7, line 3; pg 12, lines 14-15; Fig. 1-3; or Examples 1-3, as asserted by applicants.

The rejection regarding the limitation of "cloning or amplifying said nucleic acid molecule comprising a nucleotide sequence isolated from the HLA restricted CTL and encoding..." in claim 1, step c, has been withdrawn in view of the amendment.

The rejection regarding fusing any "recovered TCR receptor encoding nucleic acid molecules together to prepare the isolated fused nucleic acid molecule" (claim 1, step e) has been withdrawn in view of the amendment.

Support for step a) is found on pg 3, lines 13-18 (see citation above).

Support for step b) is found in Example 3, for example.

Support for steps c) and d) is found on pg 12, lines 10-15, and pg 13, lines 1-2. The resulting nucleic acid sequences of the α and β TCR variable regions amplified and recovered are shown in Fig. 7A and 7B.

Support for fusing the TCR α chain and β chain step to make a single chain TCR comprising a variable region of the TCR α chain fused to a variable region of the TCR β chain in step e) is found on pg 6, lines 16-18 ("Similarly, in Figure 1, construction of a single chain TCR wherein the variable regions of the α and β chains are fused through a linker and then fused to the ζ region is shown with and without the CD8 hinge").

The phrase "single chain TCR of step e comprises a TCR derivative that retains the HLA restriction and TAA-specificity characteristics of the TCR of step a" in claim 22 as newly amended has support on pg 5, lines 23-25 ("The recombinant materials relevant to the invention include those associated with the TCR produced by the nonhuman subject per se, and also derivatives of this TCR which retain their HLA restriction and specificity characteristics").

Claims 2-5 and 22 are included because they are dependent upon claim 1.

Claims 1-5 and 22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for obtaining mouse TCRs and immunizing transgenic mice that express human HLA molecules, does not reasonably provide enablement for obtaining any species of TCR other than mouse or immunizing any transgenic non-human mammal species having human HLA as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims for reasons of record.

The enablement rejection regarding the breadth of obtaining any species of TCR and immunizing any non-human transgenic species having human HLA of record (4-10-01) is maintained for reasons of record. The enablement rejection was overcome on 10-15-01, when applicants limited the claims to obtaining the α and β chains of a mouse TCR and immunizing a transgenic mouse. However, the amendment filed 7-1-02 deleted the limitation of obtaining a mouse TCR and reintroduced the breadth of

immunizing any "transgenic non-human mammal species" without marking the change to the claim. In view of the amendment filed 7-1-02 and the current amendment filed 9-24-04 which encompass obtaining any species of TCR and immunizing any transgenic non-human mammal that has human HLA, the enablement rejection regarding the breadth of obtaining any species of TCR and immunizing any non-human transgenic species of record is hereby revived. The basis of the rejection can be found in the office action of 4-10-01 on pg 5 and 6 (and previous office actions).

Claims 1-5 and 22 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The previous indefiniteness rejections have been withdrawn in view of the amendments to the claims.

The preamble of claim 1 as newly amended is indefinite because it is not commensurate in scope of the body of the claim. The preamble requires the production of a nucleic acid fusion molecule while step e results in producing a nucleic acid sequence encoding a single-chain TCR comprising a variable region of an α TCR and a variable region of a β TCR. The preamble should reflect the fact that the claim is limited to the production of a nucleic acid sequence encoding a single-chain TCR as in the body of the claim.

The preamble of claim 1 as newly amended is indefinite. TCR α and TCR β chains are narrower in scope with any non-human TCR specific for TAA. Therefore,

any non-human TCR that is specific for TAA as broadly claimed does not further limit the TCR α and TCR β chains. It is unclear if the TCR fusion protein as a whole is specific for TAA or if both the variable TCR α chain and the variable TCR β chain are specific for TAA.

Claim 1, step a, as newly amended is indefinite. It is unclear if the CLT has i) a TCR comprising a TCR α chain and a TCR β chain, wherein said TCR is specific for said TAA or ii) a TCR comprising a TCR α chain that is specific for said TAA and a TCR β chain that is specific for said TAA.

Claim 1, step e, is indefinite in view of the preamble as newly amended. It is unclear whether the single-chain fusion protein as a whole is specific for said TAA or if both the variable TCR α chain and the variable TCR β chain used to make the single-chain fusion protein are specific for TAA.

Claim 22 as newly amended is indefinite. The metes and bounds of single chain TCR comprising a TCR "derivative that retains the HLA restriction and TAA-specificity characteristics of the TCR of step a)" cannot be determined. It is unclear if the single chain must have an α chain and a β chain, each of which are human HLA restricted and TAA-specific (a narrower scope) or the if the claim is meant to encompass any single chain that is human HLA restricted and TAA-specific (a broader scope).

The prior art of record does not teach or suggest immunizing mice with TAA, obtaining CTL from the mice, cloning their variable TCR α and β chains and fusing a nucleic acid sequence encoding a variable TCR α chain with a nucleic acid sequence

encoding a variable β chain such that a nucleic acid sequence encoding a single-chain TCR is obtained. Change (1994, PNAS, Vol. 91, pg 11408-11412) and WO 95/06409 submitted in the IDS filed 11-24-04 have been reviewed in particular.

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on 571-272-0735.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

MICHAEL WILSON
PRIMARY EXAMINER